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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/434,870 | 11/04/1999 | WILLIAM D. HUSE | P-IX-3458 | 4474 |

23535 7590 10/29/2002

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| EXAMINER |
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HELMS, LARRY RONALD

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| ART UNIT | PAPER NUMBER |
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1642

DATE MAILED: 10/29/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/434,870

Applicant(s)

HUSE ET AL.

Examiner

Larry R. Helms

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 September 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 42-71 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 42-71 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

1. Claims 42-71 are pending and are currently under prosecution.
2. Claims 42, 43, 47, 48, 52, 53, 57, 58, 62, 63, 67, 68 have been amended.
3. Claims 42-71 are under examination.
4. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action

Rejections Withdrawn

5. The rejection of claims 42-71 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

Response to Arguments

6. The rejection of claims 42-71 under 35 U.S.C. 103(a) as being unpatentable over Deng et al (Canadian Patent 2,125,240 A1, published 12/7/95, IDS #8) and further in view of Yelton et al (The Journal of Immunology 155:1994-2004, 1995) and Hagiwara et al (U.S. Patent 5,589,573, issued 12/1996) is maintained.

The response filed 9/13/02 has been carefully considered but is deemed not to be persuasive. The response states that Applicants are unable to find specific

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teachings in Deng et al for CDR and framework region modifications on the same molecule (see page 12-13 of response) and none of the examples in Deng et al appear to be directed to the synthesis of antibodies with the simultaneous modification of CDR and FR residues and the response summarizes Examples 1, 2, and 3 of Deng et al (see pages 13-14 of response) and the cited pages and portions of Deng by the Examiner do not teach simultaneous randomization of CDR and FR modifications (see page 14 of response). In response to these arguments, Deng specifically teaches randomization of not only CDRs but of the frameworks also and Deng et al teach a method of humanization using randomization of exposed residues resulting in a resurfacing of the antibody and it is obvious that resurfacing would result in randomization of both framework and CDR as both of these are surface exposed residues (see page 13, lines 2-16). In addition, Yelton et al specifically teach that method are known which introduce mutations in the framework and mutations in the CDRs by error prone PCR (see page 2001). Thus it would be obvious to simultaneously produce mutations in the CDRs and in framework regions.

The response states that Deng et al does not teach the use of PCR to extend overlapping oligonucleotides and if the template DNA is to be eliminated then overlapping oligos would be used and "nevertheless, the joining of the oligos is carried out by a ligation reaction (NOT a polymerase)" (see page 15 of response). In response to this argument, as stated on page 10, lines 29-33 of Deng et al the template DNA can be eliminated by the use of overlapping oligonucleotides and as stated on page 11, lines 10-15 of Deng, if the ligase product is insufficient then the product can be amplified

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by PCR. Thus, it is obvious that if the template, wild type, is not used then the overlapping oligos can be used and amplified by PCR.

Conclusion

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be

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reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879


SHEELA HUFF
PRIMARY EXAMINER